REMARKS

I. Introduction

Claims 1-2 and 4-16 are pending in the above-identified application. All pending claims have been rejected. With this response, claims 2, 4-6, and 15 have been cancelled without prejudice, claims 1, 7-14, and 16 have been amended, and new claim 18 has been added. Favorable reconsideration and allowance of the claims in view of these amendments and the following remarks are requested.

Support for claims 1, 7, 11, and 12 as amended is found at page 1, lines 16-21 and page 3, lines 16-22. Support for claim 8 as amended is found at page 3, line 16 to page 4, line 18. Support for claims 9 and 13 as amended is found at page 4, lines 10-18. The remaining amendments and newly added claim 18 do not introduce new matter.

II. Claim Objections

Claim 2 was objected to under 37 C.F.R. § 1.75(c) as being of improper dependent form. With this response, claim 2 has been cancelled without prejudice, thereby obviating this objection.

Claims 1, 2, and 4-16 were also objected to as containing typographical errors. With this response, claims 2, 4-6, and 15 have been cancelled without prejudice, thereby obviating this objection as to those claims, and claims 7-14 and 16 have been amended to correct the identified typographical errors.

III. § 112, Second Paragraph, Rejections

Claims 1-2 and 4-16 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. The rejection of claims 2, 4-6, and 15 has been rendered moot by the cancellation of these claims.

Claim 1 is allegedly unclear as to what is "encompassed by 'controllable promoter' and 'external chemical inducer'" (Office Action of April 9, 2002, page 3). Claim 1 has been amended to recite "an inducible promoter" rather than a "controllable promoter." One of skill in the art would recognize that "an inducible promoter" refers to a promoter that may be controlled or regulated; i.e. the promoter may be turned on or off as opposed to a promoter that is turned on permanently. Further, the recitation of "an inducible promoter" clarifies the relationship between the promoter and the external chemical inducer, and one of skill in the art would recognize that the "external chemical inducer" is an exogenous chemical agent that acts to control the inducible promoter. Applicants submit these amendments overcome the Section 112, second paragraph, rejection of claim 1.

Applicants note that claims 11 and 12 have been similarly amended to recite "an inducible promoter" rather than a "controllable promoter," thereby overcoming the rejection of these claims as well.

The Examiner has suggested that claim 7 should be amended to state that the inducible promoter region "is" a chemically inducible promoter rather than "comprises" a chemically inducible promoter. Applicants respectfully disagree. As disclosed in the specification at page 3, lines 16-29, page 18, lines 1-14, and Figure 15, the inducible promoter region may include switch promoter systems. Thus, the inducible promoter region of Applicants' invention as taught in the specification is not limited to a promoter *per se*, and the Examiner's suggested amendment

unduly limits the scope of Applicants' claims. Accordingly, Applicants request the withdrawal of this rejection.

Claims 7, 9, 12, and 13 were also rejected because the use of the term "system" is allegedly unclear. With this response, the term "system" has been deleted from the rejected claims, thereby rendering this rejection moot.

Claims 9 and 13 have been rejected on the grounds that the promoter is "alcA" not "the alcA/alcR promoter system" (Office Action of April 9, 2002, page 3). Claims 9 and 13 have been amended to specify the elements of the inducible promoter region: the alcA promoter and DNA encoding the alcR regulatory protein.[1] Applicants submit these amendments overcome the Examiner's rejection.

Moreover, these amendments overcome the rejection of claims 10 and 14 by clarifying that the alcR protein forms part of the inducible promoter region recited in claims 1 and 11, respectively.

Claim 16 was rejected because the phrase "said plants" lacks proper antecedent basis. Claim 16 has been amended so as to remove the rejected language, thereby obviating this rejection. Further, amended claim 16 claims only transformed plants; progeny of these transformed plants are claimed in newly-added claim 18.

Applicants believe the foregoing amendments and remarks overcome the Section 112, second paragraph, rejections and respectfully request their withdrawal.

[1] Applicants also note that claim 8, although not rejected, has been similarly amended to specify the elements of the inducible promoter region.

IV. §112, First Paragraph, Rejections

Claims 1-2 and 4-16 were rejected under 35 U.S.C. § 112, first paragraph, on the grounds that the specification allegedly fails to enable Applicants' claimed method of increasing the yield of a plant by transforming the plant with a DNA construct comprising one or more DNA sequence(s) coding for invertase operably linked to an inducible promoter region and optionally operably linked to a transcription terminator and controlling the level, time and spatial location of expression of said DNA sequence(s) from said inducible promoter region by application of an external chemical inducer. The Examiner opines that the specification is enabling only for the specific example taught in the specification at page 18, lines 15 to 31, but does not enable the full scope of the claimed methods. Furthermore, the Examiner opines that undue experimentation would be required of one of skill in the art to: (1) determine which tissue- or organ-selective promoters expressing invertase, other than the patatin promoter, will increase plant yield; (2) identify inducible promoter systems other than the alcA/alcR system; (3) identify chemical inducers other than ethanol; and (4) determine the timing and concentration of a chemical inducer needed to induce invertase expression sufficient to increase yield (Office Action of April 9, 2002, pages 5-6).

Applicants traverse this rejection and assert the claimed invention is fully enabled by the combination of what one skilled in the art would have known as of August 8, 2000, the filing date of the instant application, and the teachings of the subject specification. Applicants' claimed invention is directed to a method of increasing the yield of a plant, comprising transforming a plant with a DNA construct comprising one or more DNA sequence(s) coding for invertase operably linked to an inducible promoter region and optionally operably linked to a transcription terminator, and controlling the level, time, and spatial location of expression of said DNA sequence(s) from said inducible promoter region by application of an external chemical

inducer. One of the examples provided in the specification (namely, the transformation of a potato plant using a construct comprising the gene encoding invertase operably linked to the alcR regulatory protein and the ethanol-inducible alcA promoter operably linked to the tuber-specific patatin promoter) merely exemplifies the claimed invention. In fact, this example demonstrates that even when a complex inducible promoter system, such as the alcA/alcR switch promoter system, is used to express invertase, enhancement of yield is observed. It is respectfully submitted that this disclosure is sufficient to enable Applicants' claimed invention under applicable legal standards. According to the *Manual of Patent Examining Procedure* (*MPEP*), "[a]s long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. 112 is satisfied. Failure to disclose other methods by which the claimed invention may be made does not render a claim invalid under 35 U.S.C. 112 [citations omitted]." *MPEP* § 2164.01(b) (8th Ed. 2001). Indeed, one need not provide any working examples. *In re Borkowski*, 422 F.2d 904 (C.C.P.A. 1970); *MPEP* § 2164.02. Thus, given that the example cited by the Examiner reasonably correlates with the scope of claim 1, it is respectfully submitted that Applicants are not required to present additional working examples of their invention.

Furthermore, Applicants would like to point out that the subject specification contains multiple working examples. For example, Applicants also teach the transformation of tobacco plants using a construct comprising the gene encoding invertase operably linked to the alcR regulatory protein and the ethanol-inducible alcA promoter operably linked to the 35S CaMV promoter (page 14, line 19 to page 16, line 2).

The Examiner also suggests that undue experimentation would be required to identify tissue- or organ-selective promoters expressing invertase other than the patatin promoter that increase plant yield. To support this argument, the Examiner cites the results reported by Bussis *et al.* (*Planta* (1997) 202:126-36) and Sonnewald *et al.* (*Plant J.* (1991) 1:95-106), which demonstrate that the constitutive expression of invertase in potato and tobacco leaves, respectively, decreases photosynthesis, as measured by a reduction in Rubisco activation state and CO_2 assimilation rate. The Examiner then opines that "[t]he down regulation of the activation state of Rubisco and the reduced rate of CO_2 assimilation, associated with the increased invertase activity, integrated over time will result in a loss of yield" (Office Action of April 9, 2002, page 5). However, Applicants maintain that the Examiner may have misapprehended these references. Bussis *et al.*, which employs Sonnewald's methodology (page 127), demonstrates that, although photosynthesis is decreased in plants transformed with invertase, the dry weight of the leaves of these transformed plants is higher than that of leaves from non-transformed plants (page 128, bottom of col. 1: "In all lines of transformants, an increased dry weight correlated with an increased starch content" & Table 2). Thus, according to these reports, invertase expression in leaves does not result in a reduction of yield. Moreover, Applicants' specification provides actual scientific results of increased yield. For example, the specification states, "[w]e have unexpectedly found that the controlled expression of an invertase gene using the alcA/alcR switch promoter system leads to an increase in plant height, an increase in leaf size and to an increase of up to 10% in the fresh weight of a plant and accelerates the time at which the plants flower i.e. the plants flower early" (page 5, lines 28-31). Accordingly, one of skill in the art, informed by Applicants' teachings of numerous tissue- and organ-specific

promoters in addition to patatin (page 4, line 23 to page 5, line 6), would be fully enabled to practice the claimed invention with a reasonable expectation of success.

The Examiner alleges that undue experimentation would be required to identify inducible promoter systems other than the alcA/alcR system taught in the subject specification. As discussed above, the subject specification describes numerous inducible promoter systems. For example, other inducible promoter systems, namely the GST promoter system and the ecdysone switch system, are disclosed in the specification (page 3, lines 16-22). These and other inducible promoter systems would have been well known to one of skill in the art at the time the instant application was filed. Thus, Applicants respectfully submit that there would be no undue experimentation for one of skill in the art to identify inducible promoter systems useful in the claimed invention.

The Examiner also alleges that undue experimentation would be required to identify chemical inducers other than ethanol suitable for use with inducible promoter systems. Applicants, however, teach alternative chemical inducers. The specification discloses that the inducible alcA/alcR promoter system controls the cellular response to "ethanol and other related chemicals" (page 9, lines 4-6), and cited publication WO 93/21334 (page 3, line 19) teaches that the alcA/alcR system may be induced using alcohols and ketones (WO 93/21334: page 5, lines 13-16). Applicants' specification, therefore, provides teachings sufficient to enable one of skill in the art to identify inducers other than ethanol for the alcA/alcR promoter system without undue experimentation. Moreover, inducible promoter systems other than alcA/alcR were known at the time the instant application was filed, such as the GST promoter and the ecdysone switch discussed above. Thus, it is respectfully submitted that undue experimentation would not

be required to identify chemically-inducible promoter systems other than the ethanol-inducible alcA/alcR system.

Finally, the Examiner opines that undue experimentation would be required to determine the timing and concentration of a chemical inducer needed to induce invertase expression sufficient to increase plant yield. Clearly, Applicants teach the timing and concentration of ethanol necessary to induce invertase expression using the alcA/alcR promoter system (*e.g.* page 14, line 27-28). One of skill in the art would be able to further determine the requisite timing and concentration of other chemical inducers suitable for use with the alcA/alcR promoter system or chemical inducers associated with different inducible promoter systems without undue experimentation. The fact that some experimentation may be required to practice the claimed invention does not warrant a rejection for lack of enablement if the required experimentation is merely routine or typical of the art. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988); *MPEP* §§ 2164.01 & 2164.06. Determining the timing and concentration of other chemical inducers needed to induce invertase expression sufficient to increase plant yield would constitute nothing more than routine optimization of Applicants' methods by one of skill in the art. Such routine optimization does not rise to the level of undue experimentation required to sustain an enablement rejection.

In view of the foregoing remarks, Applicants submit that the claimed invention is fully enabled. Accordingly, Applicants respectfully request the withdrawal of the Section 112, first paragraph, rejection of pending claims 1, 7-14, and 16.

V. § 101 Rejections

Claim 16 has been rejected under 35 U.S.C. § 101 as directed to non-statutory subject matter, because some of the claimed plant progeny would not include the transgene introduced into the parent plants and would, therefore, be indistinguishable from plants occurring in nature.

With this response, claim 16 has been amended so as to claim only the transformed parent plants, and new claim 18 has been added to claim those progeny plants that include the DNA construct introduced into the transformed parent plants, as suggested by the Examiner. The plants claimed in claims 16 and 18 differ from those occurring in nature, and, accordingly, the Section 101 rejection is overcome.

VI. § 103(a) Rejections

Claims 1-2 and 4-16 have been rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Willmitzer *et al.* (U.S. Patent No. 5,436,394) in view of Caddick *et al.* (WO 93/21334). The Examiner opines that it would have been obvious to one of skill in the art to modify Willmitzer's method with Caddick's ethanol-inducible alcA/alcR switch promoter system so as to arrive at Applicants' invention (Office Action of April 9, 2002, page 9). Specifically, the Examiner cites Caddick's teaching that the alcA/alcR switch promoter system may be used in plants as providing sufficient motivation for the combination of these references. However, because the references do not, in fact, provide the motivation required for their combination, Applicants respectfully disagree.

The claimed invention is directed to a method of increasing the yield of a plant, comprising transforming a plant with a DNA construct comprising one or more DNA sequence(s) coding for invertase operably linked to an inducible promoter region and optionally operably linked to a transcription terminator, and controlling the level, time, and spatial location

of expression of said DNA sequence(s) from said inducible promoter region by application of an external chemical inducer.

Applicants respectfully assert that the Examiner has used improper hindsight in selecting and combining the references. Upon reading Willmitzer, without the benefit of the knowledge of the present invention, one skilled in the art would learn that constitutive expression of invertase enhances plant yield. However, Willmitzer nowhere teaches or suggests that controlling the level, time, and spatial location of invertase expression using an inducible promoter increases plant yield, as claimed by Applicants. Accordingly, one of skill in the art would be completely without motivation to alter Willmitzer's method with Caddick's inducible promoter.

Even if the motivation to alter Willmitzer's method with an inducible promoter existed, which point Applicants do not concede, one skilled in the art would not select the alcA/alcR switch promoter system disclosed by Caddick. Caddick's alcA/alcR switch promoter system is complex, involving multiple elements and requiring the external chemical inducer to be taken up by the plant and transported to the tissue where the transgene is to be expressed. The likelihood of transgene expression decreases with the system's complexity. Thus, one of skill in the art would have, at most, been motivated to select an inducible promoter system less complex than the alcA/alcR switch promoter system for use in Willmitzer's method. Applicants' claimed method of increasing plant yield by transforming a plant with a DNA construct comprising one or more DNA sequence(s) coding for invertase operably linked to an inducible promoter region and optionally operably linked to a transcription terminator, and controlling the level, time and spatial location of expression of said DNA sequence(s) from said inducible promoter region by application of an external chemical inducer is, therefore, inventive. Accordingly, Applicants

respectfully request that the Examiner withdrawal the Section 103(a) rejection of pending claims 1, 7-14, and 16.

CONCLUSION

In view of the foregoing remarks, Applicants submit that all pending claims are in condition for allowance, which action is earnestly solicited.

The Examiner is invited to contact the undersigned by telephone should any issues remain outstanding.

A Petition for a one-month extension of time accompanies this response, as well as an authorization to charge the associated fee of $110.00 pursuant to 37 C.F.R. § 1.17(a)(3) to our Deposit Account No. 08-0219. No other fees are believed to be due. However, if any fees are due in connection with this application, please charge them to our Deposit Account No. 08-0219.

Respectfully submitted,

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APPENDIX OF MARKED-UP CLAIMS

1. (Once Amended) A method of increasing the yield of a plant, comprising: transforming a plant with a DNA construct comprising one or more DNA sequence(s) coding for [~~a protein involved in sucrose sensing, transport, metabolism and/or uptake operable~~] invertase operably linked to [~~a controllable~~] an inducible promoter region and optionally [~~operable~~] operably linked to a transcription terminator; [,] and controlling the level, time and spatial location of expression of said DNA sequence(s) from said [~~controllable~~] inducible promoter region by application of an external chemical inducer whereby the yield of said transgenic plant is increased.

7. (Once amended) [~~A~~] The method according to claim 1, wherein said [~~controllable~~] inducible promoter region comprises a chemically inducible promoter [~~system~~].

8. (Once amended) [~~A~~] The method according to claim 7, wherein said chemically inducible promoter is regulated by a regulatory protein, the expression of which is under the control of a tissue- or organ-selective [~~selection~~] promoter.

9. (Once amended) [~~A~~] The method according to claim 7, wherein said [~~chemically~~] inducible promoter [~~system~~] region comprises the [~~alcA/alcR promoter system~~] alcA promoter and DNA encoding the alcR regulatory protein.

10. (Once amended) [~~A~~] The method according to claim 9, wherein expression of the [~~acl R~~] alcR regulatory protein is under the control of a tissue- or organ-selective promoter.

11. (Once amended) A DNA construct comprising a DNA [~~sequence(s)~~] sequence coding for [~~a protein involved in sucrose metabolism, uptake and/or transport~~] invertase operably linked to [~~a controllable~~] an inducible promoter region.

12. (Once amended) [~~A~~] The DNA construct according to claim 11, wherein said [~~controllable~~] inducible promoter region comprises a chemically inducible promoter [~~system~~].

13. (Once amended) [~~A~~] The DNA construct according to claim 12, wherein said [~~chemically~~] inducible promoter [~~system is the alcA/alcR switch promoter system~~] region further comprises DNA encoding the alcR regulatory protein and said chemically inducible promoter is the alcA promoter.

14. (Once amended) [~~A~~] The DNA construct according to claim 13, wherein the alcR regulatory protein is under the control of a tissue- or organ-selective promoter.

16. (Once amended) Plant tissue transformed with a DNA construct according to any one of claims 11 to [~~15 and progeny of said plants~~] 14.

APPENDIX OF PENDING CLAIMS AFTER AMENDMENT

1. A method of increasing the yield of a plant, comprising: transforming a plant with a DNA construct comprising one or more DNA sequence(s) coding for invertase operably linked to an inducible promoter region and optionally operably linked to a transcription terminator; and controlling the level, time and spatial location of expression of said DNA sequence(s) from said inducible promoter region by application of an external chemical inducer whereby the yield of said transgenic plant is increased.

7. The method according to claim 1, wherein said inducible promoter region comprises a chemically inducible promoter.

8. The method according to claim 7, wherein said chemically inducible promoter is regulated by a regulatory protein, the expression of which is under the control of a tissue- or organ-selective promoter.

9. The method according to claim 7, wherein said inducible promoter region comprises the alcA promoter and DNA encoding the alcR regulatory protein.

10. The method according to claim 9, wherein expression of the alcR regulatory protein is under the control of a tissue- or organ-selective promoter.

11. A DNA construct comprising a DNA sequence coding for invertase operably linked to an inducible promoter region.

12. The DNA construct according to claim 11, wherein said inducible promoter region comprises a chemically inducible promoter.

13. The DNA construct according to claim 12, wherein said inducible promoter region further comprises DNA encoding the alcR regulatory protein and said chemically inducible promoter is the alcA promoter.

14. The DNA construct according to claim 13, wherein the alcR regulatory protein is under the control of a tissue- or organ-selective promoter.

16. Plant tissue transformed with a DNA construct according to any one of claims 11 to 14.

18. The progeny of plants regenerated from plant tissue according to claim 16, wherein said progeny comprise a DNA construct according to any one of claims 11 to 14.